LAY LANGUAGE PRECIS (Abstract)

This is a clinical trial of gene therapy for X-linked severe combined immunodeficiency (XSCID), a genetic disease caused by defects in a protein called the common gamma chain, which is normally on the surface of immune cells called lymphocytes. XSCID patients cannot make T lymphocytes, and their B lymphocytes fail to make essential antibodies for fighting infections. Without T and B lymphocytes patients develop fatal infections in infancy unless they are rescued by a bone marrow transplant from a healthy donor. However, even transplanted patients may achieve only partial immune recovery and still suffer from many infections, auto-immunity and/or and poor growth. A recent, successful trial in France used gene therapy instead of bone marrow transplantation for infants with XSCID, although leukemia occurred in two of the treated patients. This experience indicates that gene therapy has risks, but can provide clinical benefit to XSCID patients. We will enroll up to six older XSCID patients (2-20 years-old), who have previously received at least one bone marrow transplant, but still have poor T and B lymphocyte function that compromises their quality of life. Patients options and risks will be reviewed on a case by case basis prior to enrollment. The patients will have had some of their own blood-forming stem cells harvested and frozen in a blood bank. These cells have a defective gene, but a correct copy of the gene will be inserted while the cells are grown in sterile conditions outside the patient's body. To do this, the cells will be unfrozen and exposed for four days in a row to growth factors and particles of a retrovirus we have constructed and tested called "GALV MFGS-gc." Retrovirus particles will attach to the patient cells and introduce a correct copy of the common gamma chain gene into cells capable of growing into all types of blood cells, including T and B lymphocytes. Each XSCID patient enrolled in the study will receive a single dose of his own cells that have been modified by the GALV MFGS-gc treatment. After this, the patients will be monitored to find out if the treatment is safe and to see if their immune function improves. Study endpoints are (1) efficient and safe clinical-scale correction of cells from XSCID patients; (2) administration of treated cells to six subjects; and (3) 3 year follow-up of the treated subjects to see how many of their cells have taken up the correct copy of the gene, how many new T and B lymphocytes express a normal common gamma chain, and whether the patients' immune function and general health improve.